Clonidine was effective for reducing tamoxifen-associated hot flashes in postmenopausal women with breast cancer

Pandya KJ, Raubertas RF, Flynn PJ, et al. **Oral clonidine in postmenopausal patients with breast cancer experiencing tamoxifen-induced hot flashes: a University of Rochester Cancer Center Community Clinical Oncology Program Study.** Ann Intern Med. 2000 May 16;132:788-93.

QUESTION

In postmenopausal women receiving tamoxifen for breast cancer, does clonidine reduce hot flashes?

DESIGN

Randomized {allocation concealed*}†, blinded {clinicians, patients, and outcome assessors}†,* placebo-controlled trial with 12-week follow-up.

SETTING

University of Rochester Cancer Center Community Clinical Oncology Program, New York, United States.

PATIENTS

198 postmenopausal women who had received adjuvant tamoxifen therapy for breast cancer for ≥ 1 month and who reported ≥ 1 hot flash per day. Exclusion criteria were concurrent chemotherapy or other endocrine therapy for breast cancer; use of antihypertensive drugs, monoamine oxidase inhibitors, L-dopa, piribedil, tricyclic antidepressants, or sedatives; coronary insufficiency; myocardial infarction in the previous 3 months; symptomatic cardiac disease; peripheral or cerebrovascular disease; syncope; symptomatic hypertension; inability to tolerate clonidine; or abnormal renal or hepatic function. 194 women provided baseline data (mean age 54 y). Follow-up was 91% at week 4, 82% at week 8, and 75% at week 12.

INTERVENTION

After stratification for time since menopause, duration of tamoxifen therapy, and baseline frequency of hot flashes, patients were allocated to oral clonidine, 0.1 mg/d (n = 99), or placebo (n = 99) for 8 weeks.

MAIN OUTCOME MEASURES

Hot-flash symptoms (frequency; mean severity grade [score range 1 = mild to 4 = very severe]; mean duration; and combined score for frequency, severity, and duration); quality of life (self-report scale with scores ranging from 1 = worst possible life to 10 = best possible life); and side effects.

MAIN RESULTS

The clonidine group reported a greater reduction in the frequency of hot flashes at 4 weeks (mean percentage reduction 37% vs 20%, 95% CI for the 17% difference 7% to 27%) and 8 weeks (mean percentage reduction 38% vs 24%, CI for the 14% difference 3% to 27%). The reduction in the hot-flash score from baseline was greater in the clonidine group than in the placebo group at 4 weeks (mean difference in percentage reduction 18.5%, P = 0.002) and 8 weeks (mean difference in percentage reduction 18.6%, P = 0.006). Differences between groups for hot-flash severity and duration were not statistically significant at 4 and 8 weeks. The clonidine group had greater improvements from baseline in quality-of-life scores than did the placebo group at 4 weeks (mean score change from baseline 0.4 vs –0.3, P = 0.003) and 8 weeks (mean score change from baseline 0.3 vs –0.2, P = 0.022). More women in the clonidine group than in the placebo group reported difficulty in sleeping (41% vs 21%, P = 0.02).

CONCLUSION

In postmenopausal women who were receiving tamoxifen for breast cancer, clonidine was effective for reducing hot flashes.

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*See Glossary.

†Information provided by author.

COMMENTARY

The results of the study by Pandya and colleagues can be compared with those of another similarly conducted trial by the North Central Cancer Treatment Group (NCCTG) (1). This latter trial was a randomized, double-blind, placebo-controlled crossover trial (n = 116) of a transdermal clonidine preparation (1 transdermal therapeutic system).

These 2 trials had remarkably similar results. In the NCCTG trial, the intervention group had a greater reduction in hot-flash score than did the control group (mean reduction in hot-flash score 56% vs 30%, P < 0.04). In these trials, placebos were associated with hot-flash score reductions of 24% and 30%, whereas clonidine was associated with hot-flash score reductions of 42% and 56%.

Both trials noted substantially more toxicity in the patients receiving clonidine. In the study by Pandya and colleagues, clonidine was associated with greater sleeping difficulty. In the NCCTG trial, the clonidine group had substantially more trouble with mouth dryness, constipation, drowsiness, and itchiness under the transdermal patch.

Pandya and colleagues noted a statistically significant improvement in quality of life in the clonidine group. The reported 4% increase in quality of life in the clonidine group compared with a 3% decrease in the placebo group, however, is quite modest. In the NCCTG trial, a specific quality-of-life question was not addressed, although patients were asked which of the 2 treatment periods they preferred after the double-blind study periods were completed. The response to this query did not show a substantial preference for the clonidine group, presumably because of toxicity considerations. Clonidine is an option for treating hot flashes in women with breast cancer but is limited by the toxicity associated with it.

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Reference

1. **Goldberg RM, Loprinzi CL, O'Fallon JR, et al.** Transdermal clonidine for ameliorating tamoxifen-induced hot flashes. J Clin Oncol. 1994;12:155-8.